Patient-specific cells with nuclear transfer

Grant Award Details

Patient-specific cells with nuclear transfer

Grant Type: SEED Grant

Grant Number: RS1-00404

Investigator:

Name:	Aaron Hsueh
Institution:	Stanford University
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell, SCNT

Cell Line Generation: SCNT

Award Value: $629,653

Status: Closed

Progress Reports

Reporting Period: NCE

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Patient-specific cells with nuclear transfer

Public Abstract:

Somatic cell nuclear transfer (NT) is a powerful research tool with the potential for creating unique cell and tissue sources for studies of disease pathogenesis and regenerative medicine. Creation of pluripotent mouse embryonic stem (ES) cells using NT has been achieved and the prospects for generating human ES cells by NT are promising. However, there are only a handful of researchers who have reported their experience with NT and development of this approach in California would benefit from increasing dedicated efforts toward this goal. We have assembled a team focused on NT that has achieved several experimental milestones that motivate these proposed studies of NT in human oocytes. These prior achievements include NT in mouse oocytes, efficient production of novel ES cells from mouse embryos, and controlled enucleation of recipient human oocytes. With CIRM SEED funds, we will use systematic approaches to identify conditions that generate multipotent human cells from NT into human oocytes, with the goal of eventually producing new patient-specific human ES cell (hESC) lines for studies of disease pathogenesis, transplantation and tissue regeneration.

Successful outcomes from this proposal would enable us and others to generate new ES cell lines to study the pathogenesis of human diseases. Discovery of molecular mechanisms underlying diseases inevitably will produce novel strategies for diagnosis, prognosis or therapeutics. For instance investigators here have provided evidence for dysregulated signaling through the NFAT/calcineurin pathway in Down syndrome (DS), which arises in patients with trisomy for chromosome 21. Development of diagnostics or therapies that exploit the tenets of this model would surely be accelerated by tests of the model with embryonic human tissue harboring the classic trisomy 21 karyotype. Currently, such embryonic tissues for experimental studies are not available we postulate that a human DS ES cell line generated by NT could be used to develop differentiating embryonic human tissues for study of dysregulated signaling in vitro. Similar logic would justify generating patient-derived ES cell lines to produce experimental systems for studies of other diseases, including childhood congenital malformations, sickle cell disease, or neurological disorders lacking models or a defined pathophysiologic basis, like amyotropic lateral sclerosis (ALS).

Statement of Benefit to California:

The generation of ES cell lines by nuclear transfer can be inefficient, and initial attempts to produce nuclear-transfer-derived blastocysts from human somatic donor cells have been unsuccessful. There are only a handful of researchers who have reported their experience with somatic cell nuclear transfer (SCNT) and development of this approach in California would benefit from increasing dedicated efforts toward this goal. Successful outcomes from the research proposed here would identify California as a center of nuclear reprogramming and SCNT. California institutions would benefit from the ability to create unique patient-specific embryonic stem cell lines and disease models from SCNT. In turn, this would accelerate progress in developing new therapeutic and diagnostic strategies for diverse human disorders. Progress in this area would attract researchers and others interested in using stem cells for disease study and treatment. Ultimately, these positive effects would likely improve human health in California and elsewhere.
